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APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.	CONFIRMATION NO.
08/278,601	07/21/1994	DAVID KNIPE	DFCI363A	6837

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GEORGE W. NEUNER
EDWARDS & ANGELL, LLP
P. O. BOX 9169
BOSTON, MA 02209

EXAMINER	
MOSHER, MARY	
ART UNIT	**PAPER NUMBER**
1648	44

DATE MAILED: 04/06/2004

Please find below and/or attached an Office communication concerning this application or proceeding.

Office Action Summary	Application No.	Applicant(s)	
	08/278,601	KNIPE ET AL.	
	Examiner	Art Unit	
	Mary E. Mosher, Ph.D.	1648	

-- The MAILING DATE of this communicati n appears on the cover sheet with the correspondence address --

Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE 3 MONTH(S) FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If the period for reply specified above is less than thirty (30) days, a reply within the statutory minimum of thirty (30) days will be considered timely.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133). Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

1)☐ Responsive to communication(s) filed on *09 July 2003*.

2a)☐ This action is **FINAL**. 2b)☒ This action is non-final.

3)☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disp sition of Claims

4)☒ Claim(s) *12-21,31,36,41 and 50-96* is/are pending in the application.

4a) Of the above claim(s) _____ is/are withdrawn from consideration.

5)☐ Claim(s) _____ is/are allowed.

6)☐ Claim(s) *12-20,,31,36,41,50-74 and 76-96* is/are rejected.

7)☐ Claim(s) *21 and 75* is/are objected to.

8)☐ Claim(s) _____ are subject to restriction and/or election requirement.

Application Papers

9)☐ The specification is objected to by the Examiner.

10)☐ The drawing(s) filed on _____ is/are: a)☐ accepted or b)☐ objected to by the Examiner.

Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).

Replacement drawing sheet(s) including the correction is required if the drawing(s) is objected to. See 37 CFR 1.121(d).

11)☐ The oath or declaration is objected to by the Examiner. Note the attached Office Action or form PTO-152.

Priority under 35 U.S.C. § 119

12)☐ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).

a)☐ All b)☐ Some * c)☐ None of:

1.☐ Certified copies of the priority documents have been received.

2.☐ Certified copies of the priority documents have been received in Application No. _____.

3.☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

* See the attached detailed Office action for a list of the certified copies not received.

Attachment(s)

1) ☒ Notice of References Cited (PTO-892)
2) ☐ Notice of Draftsperson's Patent Drawing Review (PTO-948)
3) ☐ Information Disclosure Statement(s) (PTO-1449 or PTO/SB/08) Paper No(s)/Mail Date _____.
4) ☐ Interview Summary (PTO-413) Paper No(s)/Mail Date. _____ .
5) ☐ Notice of Informal Patent Application (PTO-152)
6) ☐ Other: _____.

DETAILED ACTION

Response to Amendment

In the amendment filed July 9, 2003, claim 41 was both amended and cancelled. The examiner assumes that the intent was to cancel claims 42-49; please confirm if that was the case.

Claims 12-21, 31, 36, 41, and new claims 50-96 are pending.

In the interference as redeclared on May 18, 2001, the count (as it pertained to this applicant's claims) read:

A method of immunizing a mammal comprising administering to said mammal a vaccine comprising a mutated herpesvirus capable of infecting a mammalian cell and of eliciting a protective immune response upon administration, said herpesvirus having a mutation in one of more genes encoding a protein essential for viral replication to render the herpesvirus replication defective, wherein the mutation is in the gene or genes encoding the proteins ICP8 or ICP27 (claim 35, rewritten with the limitations of parent claim 32)

Or

A method of inducing an immune response against herpesvirus in a mammal comprising administering to said mammal a vaccine comprising a mutated herpesvirus, said herpesvirus having a mutation in one or more genes encoding a protein essential for viral replication to render the herpesvirus replication defective, wherein the mutation is in the gene or genes encoding the proteins ICP8 or ICP27 (claim 40, rewritten with the limitations of parent claim 37).

The interference contest was abandoned, and claims 1-9, 25-27, 29, 32-35, 37-40, and 42-49, corresponding to the count, stand finally disposed of. The Board has determined that applicant is not entitled to a patent upon the subject matter of those claims.

Claims which did not correspond to the count were claims 12-22, 31, 36, and 41. During the interference proceedings, claims 12-17 involved "a method of treating an immunomodulatory disease" with a mutant herpesvirus "having an ability to effect a subclass shift of IgG2a/IgG upon in vivo administration to a mammal". Claims 18-22 involved similar treatment method using a virus "having an ability to produce IFN-gamma upon administration." Claims 31, 36, and 41 involved a virus encoding one or more heterologous genes.

With the response filed July 9, 2003, claims 12 and 17 have been amended to delete all of the elements which rendered them distinct from the lost count. Claims 16 and 18 have been amended to delete one of the two elements which rendered them distinct from the lost count. Claims 31, 36, and 41 retain the "heterologous gene" element which rendered them distinct from the lost count.

Claim Rejections - 35 USC § 112

Claims 50-70, 73, 74, and 76-96 are rejected under 35 U.S.C. 112, first paragraph, as containing subject matter which was not described in the specification in such a way as to reasonably convey to one skilled in the relevant art that the inventor(s), at the time the application was filed, had possession of the claimed invention. This is a "new matter" rejection. Applicant indicates that claims 50-68 are

added from copending application 08/903,830, and claims 68-96 are added from copending application 09/034,464. Applicant further states that the present application has the same specification as the copending applications. However, this is not correct. Both 08/903,830 and 09/034,464 were continuations-in-part of this application. This application has no disclosure of the "UL5" subject matter now claimed. Applicant is also requested to point to support in this specification for the specific combination of nonsense with deletion mutations as recited in new claims 53, 60, 65, 67, 76, 87, 90, 93, 95, and the "B-cell and/or T cell response" in new claim 96.

Claims 64, 65, 70-72, 74, 76 are rejected under 35 U.S.C. 112, second paragraph, as being indefinite for failing to particularly point out and distinctly claim the subject matter which applicant regards as the invention. Claims 64 and 65 are confusing, being drawn to a composition but depending from a method claims. Claim 70 recites the limitation "the protein essential for replication". There is insufficient antecedent basis for this limitation in the parent claim. This affects dependent claims 71-72. Claims 71 and 72 are also confusing in that it is not clear if "the protein" means "the protein essential for replication" in parent claim 70, or the "heterologous protein" in claim 68. In claim 74, "said proteins for replication" lacks antecedent. Also in claim 74, it is not clear what is meant by adding the requirement for "immediate early or early genes", is the intent to exclude the UL5 member of the Markush group recited in parent claim 73? Claim 76 is indefinite because it depends from cancelled claim 6; is claim 68 intended?

Claims 31 and 36 are rejected under 35 U.S.C. 112, second paragraph, as being indefinite for failing to particularly point out and distinctly claim the subject matter which applicant regards as the invention. The preamble of the claims recites "A vaccine", which ordinarily means a composition capable of inducing an immune response protective against disease. However, in the body of the claims, the active steps require a virus capable of "eliciting an immune response to heterologous gene products." Therefore, it is not clear if the scope of the claim is a composition which elicits an immune response, or a vaccine composition which elicits a protective response.

Claims 16-20 are rejected under 35 U.S.C. 112, first paragraph, because the specification, while being enabling for a method of treating herpes stromal keratitis using a herpesvirus which elicits an IgG2a/IgG1 subclass shift or induces production of IFN-gamma, does not reasonably provide enablement for treatment using any replication defective herpesvirus. The specification does not enable any person skilled in the art to which it pertains, or with which it is most nearly connected, to practice the invention commensurate in scope with these claims. The specification teaches that replication defective herpesviruses capable of eliciting IgG2a/IgG1 subclass shift or inducing IFN-gamma are useful in treating herpetic stromal keratitis, see specification page 14. The specification also teaches that some replication defective herpesviruses do not induce the subclass shift, see pages 50-51. Therefore, the specification does not teach how to use the full scope of replication defective herpesviruses to treat herpetic stromal keratitis.

Claim R jections - 35 USC § 102

Claims 12-15 are rejected under 35 U.S.C. 102(g) or, in the alternative, under 35 U.S.C. 103(a), as being drawn to the same invention as the lost count, or on the grounds of estoppel. Claim 12 has been amended to remove the "immunomodulatory disease" and "subclass shift" subject matter which rendered it distinct from the interference count. Now the key elements of the claim are that the herpesvirus administered to a mammal has a mutation in a gene essential for viral genome replication, and the virus is in a pharmaceutically effective carrier. Dependent claims 13-15 further limit the subject matter to HSV, and the genes ICP8 and/or ICP27. The subject matter of amended claim 15 is identical to the subject matter of lost claim 35 (except for the carrier). It is noted that claim 15 depends from a claim which recites "essential for viral genome replication", and the lost count depended from a claim which recited "essential for replication" and was silent upon *genome* replication. However, a method of immunizing a mammal using an HSV defective in ICP8 or ICP27 is the same method, regardless of whether ICP8/27 are characterized as "essential for replication" or "essential for genome replication." The final judgment in interference was that applicants were not entitled to a patent on the method of claim 35; characterizing the ICP8 or ICP27 mutation as "essential for viral genome replication" in the preamble of the parent claim does not overcome the judgment and final disposal of this claimed subject matter.

Similarly, claims 50-64, 66 are rejected under 35 U.S.C. 102(g) or, in the alternative, under 35 U.S.C. 103(a), as being drawn to the same invention as the lost

count, or on the grounds of estoppel. These claims, by including ICP27 and ICP8 in the Markush group of mutations in the claimed compositions and methods, encompass subject matter which the Board has ruled unpatentable to this applicant.

Claim Rejections - 35 USC § 102

Claims 36 and 41 are rejected under 35 U.S.C. 102(b) as being anticipated by Dobson et al (Neuron 5:353-60, 1990). Dobson teaches a herpesvirus with a mutation in the ICP4 gene essential for viral genome replication, comprising a heterologous gene. Dobson teaches a composition comprising the virus and administration of the composition to a mammal. The reference does not teach that the virus is capable of eliciting an immune response against the herpesvirus or against the heterologous product, however these are inherent capabilities. This rejection could be obviated by amending the claims to require the heterologous gene to encode an antigen of a pathogen.

This rejection is not applied to claim such as claim 31 which involve a composition "in a pharmaceutically accepted carrier." Dobson is silent upon the carrier used to administer the defective herpesvirus to the mammal, and an argument could be made that the undisclosed carrier is inherently pharmaceutically acceptable. However, considering the degree of purity, control of starting materials, and documentation required for pharmaceutically acceptable materials (as evidenced by Cartwright, Tibtech 5:25-30, 1987), the examiner considers it unlikely that any viral carrier medium used by Dobson would be pharmaceutically acceptable. Therefore the examiner is unable to meet the burden required to reject these claims on the grounds of inherent anticipation.

However, applicant may wish to amend the claims to clarify that the heterologous gene encodes an antigen of a pathogen, so as to avoid any confusion as to whether the claims read upon viruses encoding products intended for gene therapy.

Claim Rejections - 35 USC § 103

The rejection of claims 31, 36, and 41 under 35 U.S.C. 103(a) as being unpatentable over Inglis et al WO 92/05263 in view of McCarthy et al (Journal of Virology 63:18-27, 1989) is withdrawn on reconsideration. Applicant agues that Inglis is not prior art, because the instant invention claims priority to July 31, 1992. This argument is not convincing because the Inglis patent was published April 2, 1992, which is prior to July 31. However, on reconsideration, Inglis emphases that a block after genome replication is advantageous for developing an immune response, e.g. page 8, lines 9-20, page 10 line 17- page 11 line 10, page 13 lines 19-23. Inglis does teach that human cytomegalovirus can be blocked prior to genome replication, see page 9, lines 2-12. However, in the context of the rest of the paragraph and the preceding paragraph, Inglis appears to be discussing an immunogenic response directed against the defective herpesvirus itself. Inglis has no specific discussion regarding combination of a heterologous gene with mutation blocking genome replication. Considering the teachings of Inglis as a whole, use of a herpesvirus blocked prior to genome replication for an immunogenic expression vector is seen as obvious to try, at best. Furthermore, in regard to claim 41, Inglis fails to provide motivation for including a heterologous gene in an anti-herpes immunogen, in the absence of impermissible hindsight.

Allowable Subject Matter

Claims 21 and 75 are objected to as being dependent upon a rejected base claim, but would be allowable if rewritten in independent form including all of the limitations of the base claim and any intervening claims.

Conclusion

Any inquiry concerning this communication or earlier communications from the examiner should be directed to Mary E. Mosher, Ph.D. whose telephone number is 571-272-0906. The examiner can normally be reached on M-T and alternate F.

If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, James Housel can be reached on 571-272-0902. The fax phone number for the organization where this application or proceeding is assigned is 703-872-9306.

Information regarding the status of an application may be obtained from the Patent Application Information Retrieval (PAIR) system. Status information for published applications may be obtained from either Private PAIR or Public PAIR. Status information for unpublished applications is available through Private PAIR only. For more information about the PAIR system, see http://pair-direct.uspto.gov. Should you have questions on access to the Private PAIR system, contact the Electronic Business Center (EBC) at 866-217-9197 (toll-free).

4/1/04

MARY E. MOSHER
PRIMARY EXAMINER
GROUP 1800 1600